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Risperidone Induced Xerosis and Tachycardia in Schizophrenia Patients: A Case Report

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ABSTRACT
Background: Risperidone is one of the atypical antipsychotics usually used in schizophrenia therapy. Like most antipsychotics, risperidone has several side effects. Xerosis and tachicardy are rare side effects of Risperidone with incidence <1%. However unfortunately, the numbers of case reports about risperidone's side effects are very limited, especially in Indonesia. The case report aims to inform the health professionals about the side effect of risperidone in Schizophrenia patienst in Indonesia.
Case presentation: A 54-year-old woman was hospitalized with a diagnosis of schizophrenia. The patient received risperidone 2mg, clozapine 25mg, 1/2 ampule haloperidol injection, cetirizine 10mg, methylprednisolone 4mg, amlodipine 5mg. On the following day, the patient experienced itching, hardening of the facial skin and tachycardia (pulse 124). The Naranjo score for riperidone was 6 (probably). After the incident, the physicians stopped the risperidone. The patient was then prescribed a facial lotion to treat her dry and peeling facial skin. After discontinuing the risperidone, the patient's facial skin condition improved, and the pulse was normal.
Conclusion: Risperidone is known to have side effects of xerosis and tachycardia in these patients, so healthcare professionals should monitor the use of risperidone and other antipsychotics to anticipate potential side effects.

Keywords: *risperidone, schizophrenia, side-effects, tachycardia, xerosis*

1. BACKGROUND

According to WHO, Schizophrenia is a mental illness characterized by disturbances in thinking, emotional disorders, language, taste, and behavior. The symptoms of schizophrenia include delusions and hallucinations. Schizophrenia affects nearly 20 million people. Management of Schizophrenia is carried out using pharmacological and non-pharmacological therapies that involve: psychiatrists, psychologists, families, and of course, pharmacists ***[1]***.

Pharmacological therapy for schizophrenia usually uses antipsychotics. The choice of antipsychotic depends on the type of schizophrenia, the patient's condition, and many other factors that vary from patient to patient. Remington et al. (2017) divided schizophrenia therapy based on six conditions, namely

1. Early episodes
2. Acute exacerbations
3. Relapse prevention and maintenance therapy
4. Resistant therapy
5. Clozapine resistance.
6. Specific domain symptoms ***[2]***

The choice of antipsychotics used in therapy also depends on the patient's condition, thus there is no definite therapeutic algorithm. In the moment of administering pharmacological therapy, counseling to patients is needed, especially regarding side effects. Antipsychotic drugs have many side effects. The side effects that occur can be acute (dizziness, sedation, and anxiety) or delayed side effects such as cognitive impairment. These side effects frequently aggravate the patient's condition so that the patient often becomes non-adherence to the therapy ***[3]***.

Risperidone is one of the antipsychotics that is often used in schizophrenia. Some side-effects of risperidone are categorized as common or very common (>10%), uncommon (1%-10%), and rare (<1%). Some studies reported the side-effects of risperidone like fatigue, somnolence, tremor, weight gain, tachycardia, unclassified erythema with a variation of incidence [4–6].

Many patients are not well educated about this drug's side effects. Therefore, this case report was written to provide additional information on the incidence of antipsychotic side effects. This information is expected to become educational material for health workers, patients, and their families who use antipsychotics.

2. CASE PRESENTATION

The patient, a 56-year-old woman, was hospitalized on November 4, 2019, at 05.10pm. The patient was taken by his family because she was angry, rowdy, anxious, confused, went out of the house, bought clothes, talked to herself, and attacked people with words. Her history was stage 2 hypertension. At admission, blood pressure was 180/84mmHg, pulse 95x/minute, temperature 36.3ºC, and

Respiratory Rate (RR) 20x/minute. The patient was diagnosed with Undifferentiated schizophrenia [7]. The patient was treated with risperidone 2mg, clozapine 25mg, haloperidol injection 1/2 amp, cetirizine 10mg, methylprednisolone 4mg, amlodipine 5mg. The data of patient progress can be seen in table 1.

Table1. Patient Progress

Day	Drugs	Condition	BP (mm/Hg)	RR(x/minute)	P(x/minute)	T(^{0}C)
1	Risperidone 2mg Clozapin 25mg Haloperidol inj 1/2 amp Cetirizine 10 mg, Methylprednisolone 4mg Amlodipine 5mg	angry, rowdy, anxious, confused, went out of the house, bought clothes, talked to herself, and attacked people with words	180/84	20	95	36.3
2	Risperidone 2mg, Lorazepam 0,5mg, Amlodipine 5mg Methylprednisolone 4mg Cetirizine 10mg **Clozapine stop**	Enough sleep rest, much progress, a negative sign of violent behavior, relatively calm, and cooperative. The patient began to **feel itchy, and the face felt hard.** The nutritional status based on the upper arm's circumference was insufficient; the food intake was sufficient.	164/84		117	36.2
3	injection of haloperidol 1 amp im /12 hours, Tri Hexy Phenidyl (THP) 2mg, Lorazepam 0.5mg, Clozapine 100mg Face lotion **Risperidone stop**	The patient's condition deteriorated, spoke curtly, lacked rest, was angry, had a ½ portion of the diet, and behaved violently. She wanted to go home and became less cooperative and autistic. Facial skin began to peel, and physical complaints increased.	122/90	20	124	36.2
4	Facial lotion, Amlodipine 5mg , Methylprednisolone 4mg Haloperidol 1.5mg THP 2mg, l Lrazepam 0.5mg, Clozapine 100mg, Haloperidol injection1 amp/24 hours. **Cetirizine stop**	The patient behaved violently and felt her face blackened due to occult knowledge, lacked rest, was restless, paced, inter-magic, hallucination, and autistic, while physical complaints reduced. The patient was still at his own pace, insistent, well-spoken, and somewhat temperamental				
5	Haloperidol 1.5mg THP 2mg, Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	The patient began to calm down, cooperative, positive audio and visual hallucinations, unrealistic, and poor insight. There were no physical complaints, and itching on the cheeks had improved. She got enough rest, autistic, and had sensory perception disorders	139/86			
6	Haloperidol 1.5mg THP 2mg, Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	The patient had enough rest, irritability, worried expression, directed behavior, at will, pacing, risk of violent behavior, sensory perception	125/83		103	
7	Haloperidol 1.5mg THP 2mg, Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	The patient was unstable and spoke harshly, had adequate rest, the risk of violent behavior and sensory perception disorders, lack of nutrition, and good food intake	113/97	20	91	36.5
8	Haloperidol 1.5mg THP 2mg,	The itching on the patient's cheeks improved. The patient wanted to take morning				

	Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	medication such as haloperidol 5mg, and lorazepam 0.5, while in the evening haloperidol 5mg, THP 2mg, and clozapine 100mg. There was a synergy drug interaction between lorazepam and clozapine, with the risk of cardiorespiratory cholars. Clozapine increased the QT interval, where there was an antidopaminergic effect.				
9	Haloperidol 1.5mg THP 2mg, Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	The patient was still autistic, irritable, and suspicious, had lots of requests, adequate rest, and was not motivated yet. The risk of violent behavior and sensory perception disorders was still there.	131/75	18	89	
10	Haloperidol 1.5mg THP 2mg, Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	The patient became autistic, irritable, suspicious, demanded, rested, unmotivated, and risked violent behavior. Furthermore, the patient was autistic, pacing back and forth, talking to herself, sleeping, diet 1/2	122/78		81	
11-13	Haloperidol 1.5mg THP 2mg, Lorazepam 0.5mg, Clozapine 100mg Amlodipine 5mg	The patient could sleep enough in the next two days, autistic, at will, pacing, guided, signs of negative, violent behavior	126/75		86	
14	Haloperidol 1.5mg Risperidone 2mg, THP 2mg, Clozapine 100mg, valproic acid 250mg **Lorazepam stop Risperidone regiven**	She, got enough sleep but still paced all night, hallucination	131/66	20	88	36.3
15-22	Haloperidol 1.5mg Risperidone 2mg, THP 2mg, Clozapine 100mg, Valproic acid 250mg	The patient's condition was calm, cooperative enough; and cooperative; hallucinations sometimes appeared,, and she had adequate rest	108/69	18	92	36.1
24	Take home medicine : Risperidone 2mg, Haloperidol 1.5mg, THP 2mg, Valproic acid 250mg Clozapine 100mg	By the time she went home on November 28, the patient had enough sleep, was calm, cooperative, and straight.; She wanted a diet, drugs	117/63	18	100	36.1

3. DISCUSSION

Risperidone is a second-generation antipsychotic. Its mechanism of action is to block 5-HT receptors and dopamine D2 antagonists. In the UK, risperidone is licensed to treat psychotic conditions with prominent positive and negative symptoms, for maintenance therapy in patients responsive to risperidone, and mania in bipolar disease [4]. In Indonesia, risperidone has a distribution license for acute and chronic psychosis and mania [8].

For the first time, the drug given to this patient was a combination of 3 antipsychotics, namely risperidone, clozapine, and haloperidol. The use of a combination of 3 antipsychotics is common, which is tailored to the patient's condition [9]. Clozapine was most likely given as the patient showed no response or responded partially to other antipsychotics. The use of 3 antipsychotics in this patient was due to the patient's restless condition, lack of sleep. Risperidone, clozapine, and haloperidol can overcome patient agitation. Combinations of these three drugs are allowed in cases of unresponsive or partial response patients [3,10].

When clozapine was stopped, the patient experienced deterioration in condition, and agitation led to violent behavior. The patient was still given risperidone and haloperidol. The patient had xerosis on the second day after therapy. Xerosis is a condition in which the skin becomes dry, rough, scaly, and easily peels off. Xerosis usually occurs due to a lack of moisture and hydration in the skin. The contributing factors include age, conditions of menopause, and the use of certain drugs. Xerosis is a secondary feature of

many conditions. Risperidone is the only precipitating factor for various causes of xerosis. Based on tracing medical records, it was found that the patient did not have diabetes, which was a risk factor for xerosis, the patient also did not take diuretics, and there was no history of psoriasis [11,12]. Tracing drug interactions also did not reveal the possibility of xerosis. From the literature study, the most likely cause of xerosis is risperidone. On evaluation with the Naranjo scale, we obtained score fpr risperidone was 6 (probable association between drug and side-effects), and for clozapine, THP, haloperidol were 2 (possible)[13]. The mechanism which risperidone causes xerosis is not known.

The incidence of xerosis with risperidone was not known with certainty, only <1% was mentioned, so it is a rare side effect [4,14]. The patient's xerosis improved with facial lotion therapy and discontinuation of risperidone. Risperidone was just given back on November 18 (1-day discontinuation). Risperidone was regiven as the patient still having hallucinations with clozapine and haloperidol.

Another side effect of risperidone that occurred in this patient was tachycardia. On table.1 we can see the patient experienced an increase in heart rate (95x/minute to 124x/minute) Tachycardia has an incidence of 1% -5% in adults and can occur immediately after drug administration. In the Turkoz study, et al., tachycardia's incidence rate was 1% with risperidone 2-4mg / day and increased to 3% at 4-6mg / day. The likelihood of tachycardia might increase if the dose increased [14–16].

These two side effects were not the significant side effects of risperidone but occurred in this patient. In the case of the patients in this study, the xerosis and tachycardia improved after discontinuation of risperidone.

When risperidone stopped, clozapine was given as the patient still experience hallucinations. Once the patient rested sufficiently, lorazepam discontinued. The patient was given valproic acid to control the patient's aggressive condition. Valproic acid interacts with risperidone and can increase risperidone toxicity, so close monitoring is warranted [14] The patient went home on November 28th with home medication risperidone, haloperidol, valproic acid, clozapine, and THP. This condition requires counseling from a pharmacist regarding possible recurrence of side effects, increased risperidone toxicity, and patient's non-compliance. In table 1, it can be seen that an increase in heart rate began to be seen after risperidone was given again on day 14 (Pulse = 88x / minute) to 100x / minute on return. Furthermore, counseling should involve the patient and the patient's family.

4. CONCLUSION

In this patient, xerosis and tachycardia were found, which were side effects of risperidone. Pharmacists should closely monitor these side effects because risperidone was regiven

AUTHORS' CONTRIBUTIONS

All authors contributed to data collection, data analysis, and writing of this manuscript

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